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**1,139,188**



# PATENT SPECIFICATION

NO DRAWINGS

**1,139,188**

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Int. Cl.:—A 61 k 3/00

## COMPLETE SPECIFICATION

### Germicidal Compositions comprising 1-Bromo-3-Chloro-5,5-Dimethyl Hydantoin

I, LUIS MANUEL GARCIA PADILLA, of Chapultepec Avenue No. 273, Mexico, D.F., Mexico, of Mexican nationality, do hereby declare the invention, for which I pray that a patent may be granted to me, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention concerns processes and compositions for combating germs and, more particularly, it concerns a wide spectrum germicidal composition for combating a great number of germs pathogenic to both animals and humans.

Many ailments affecting warm-blooded animals, including human beings, heretofore have been difficult to cure or prevent using antibiotics since known wide spectrum antibiotics, because of their histaminic action, have caused a great number of individuals to become sensitive thereto and the several strains of germs attacked thereby tended to become resistant, so that these antibiotics tended to lose their efficiency in a short time.

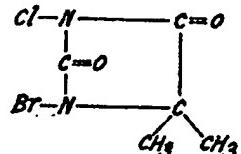
Therefore, it has been desirable for a long time to find a medicinal product which, without being an antibiotic or functioning as such, was highly efficient in killing germs in warm-blooded animals without causing allergic reactions or creating organic defences in the germs which in the long run would make them resistant.

It has now been discovered that 1-bromo-3-chloro-5,5-dimethyl-hydantoin is a germicidal chemical compound which, when applied through different routes in warm-blooded animals, exerts a germ-killing action. It is not an antibiotic. Antibiotics have a chemical structure similar to that of a vitamin or other vital element necessary for the development of germs.

As is well known, all chemical compounds of the prior art, used to kill germs, are

chemotherapeutics or antibiotics. These compounds are absorbed by the germs, instead of some vitamins or other compounds vital to the growth of the germ. They thus "deceive" the genetic code provided by the DNA of the germs, with the result that some proteins or other compounds necessary to the growth of the micro-organism are not produced so that the micro-organism dies through failure to synthesize the compounds necessary for its development. However, these chemotherapeutics or antibiotics have been also observed to cause acute allergic responses in warm-blooded animals.

In accordance with the present invention there is provided a wide spectrum germicidal therapeutic composition for use in combating infectious diseases in warm-blooded animals, including humans, comprising a germicidally active proportion of 1-bromo-3-chloro-5,5-dimethyl-hydantoin of the formula:



and a pharmacologically acceptable carrier therefor, but excluding solutions of the hydantoin in water or an organic solvent. The compositions may be administered either topically, orally or parenterally, and have an immediate action on many types of germs or micro-organisms.

The invention also provides a method for treating germ-caused ailments in non-human warm-blooded animals, which comprises administering parenterally, topically or orally to the animal a germicidal amount of 1-bromo-3-chloro-5,5-dimethyl-hydantoin of the formula:

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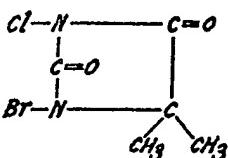
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in a pharmacologically acceptable carrier.

5 Preferably the pharmacologically acceptable carrier is a polyalkylene-glycol e.g. polyethylene glycol, polypropylene glycol, or polybutylene glycol.

It may also be an aqueous medium. In this case the compositions comprise vitamins A and D in addition to water. Preferably the proportion of hydantoin used is from 0.005 to 1.0% by weight with respect to the total weight of the hydantoin and carrier.

One embodiment of the invention comprises a composition of matter containing 0.033% by weight of 1-bromo-3-chloro-5,5-dimethylhydantoin in an aqueous vehicle, to be used as a medicament for topical application, particularly for ocular application.

According to a particularly preferred embodiment of the invention, a composition of matter is provided comprising 0.1% by weight of the active ingredient in an aqueous vehicle, said composition being highly useful in providing germicidal action when topically applied for instance, to ears, nose or throat, as well as when applied intraperitoneally, rectally and vaginally.

Another preferred composition of the present invention can be parenterally administered by injection, and comprises 0.01% by weight of 1-bromo-3-chloro-5,5-dimethylhydantoin in an oily vehicle such as a polyalkylene glycol. The composition is highly useful for intravenous, intraperitoneal and even intraarterial application.

In accordance with another embodiment of the present invention, a composition of matter for external use can also be prepared, more or less similar to the above mentioned parenteral composition, but in this particular case comprising suitable proportions of vitamins A and D, in order to avoid the dry sensation caused, inter alia, in the mucosa.

45 All compositions of matter described in the foregoing, have been tested in several animals suffering from different ailments, and it

has been found that compositions of the invention have a wide spectrum action, and their toxicity is negligible when administered to warm-blooded animals, in suitable doses.

Compositions of matter in accordance with the present invention, because of the active ingredient which they contain, are highly effective in treating such ailments as bovine mastitis, enteritis in hogs, polyarthritis and many other ailments produced by pathogenic micro-organisms which attack warm-blooded animals, including men.

In order to give a complete and clear idea of the wide spectrum activity of the active ingredient of compositions in accordance with the present invention, and of the processes used for the treatment of different ailments, the following illustrative Examples will be given to disclose several applications to which the 1-bromo-3-chloro-5,5-dimethyl-hydantoin can be put in the field of veterinary and human medicine.

## **EXAMPLE I BOVINE MASTITIS**

Mastitis is a very common ailment in the world, and is statistically considered as the one which is most destructive towards milk production in several regions of the world, especially in tropical regions.

Mastitis is caused by pyogenic germs, for instance the species *pyogenes*, *Agalactiae*, *Disgalactiae* and *Uberis* of the genus *Streptococcus* or the species *aureus* of the genus *Staphylococcus*.

The treatment heretofore used for curing this very widespread ailment is based on the application of antibiotics and chemotherapeutic substances either singly or combined with papain, corticosteroids and even trypsin, in doses which are administered at intervals of 24 hours during 2 to 3 days.

A group of 8 milk cows from a region of Cuautitlan, State of Mexico, Mexico, were selected and treated through the intramammary route, by means of a syringe and udder probe and in some cases by means of a cannula adapted to a plastic blower, with a composition of matter comprising 0.01% of 1-bromo-3-chloro-5,5-dimethyl-hydantoin, dissolved in a sufficient amount of polyethylene glycol.

The results obtained by these tests are summarized in Table I below:

TABLE I

Cow	No.	Therapy			Secondary Effects
		Daily Dose	Duration	Results	
1	5	20 c.c.	1 day	Full recovery	None
2	23	20 c.c.	1 day	Full recovery	None
3	11	20 c.c.	2 days	Full recovery	None
4	30	20 c.c.	2 days	Full recovery	None
5	33	20 c.c.	2 days	Full recovery	None
6	62	20 c.c.	2 days	Full recovery	None
7	82	20 c.c.	2 days	Full recovery	None
8	103	20 c.c.	2 days	Full recovery	None

It can be concluded from an inspection of the above Table, that out of the 8 treated cows, 100% fully recovered. 2, i.e. 25% of the above mentioned cows, which are listed under numbers 1 and 2, only required treatment for 1 day to be cured.

The remaining cows recovered after the two days, so that the maximum curative dose was 10 4 milligrams administered in two applications of 2 milligrams every 24 hours.

**EXAMPLE II**  
**ENTERITIS IN HOGS**

Enteritis (diarrhea) is a very common ailment in hogs and causes weight loss, poor de-

velopment and even death through dehydration, particularly in suckling pigs.

The most common form of enteritis in hogs is caused by germs of the family Enterobacteriaceae, particularly by species of the genera Escherichia and Salmonella.

Hitherto the treatment for curing this ailment has not been very satisfactory.

For the following tests 12 pigs were selected from the region of Ocotepec, Morelos State, Mexico, and treated with 0.03% by weight of an aqueous solution of 1-bromo-3-chloro-5,5-dimethyl-hydantoin.

The doses used, and the results of the experiments, are as listed in Table II below.

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TABLE II

Pig No. (Mean weight 20 kg.)	Therapy			Results	Remarks
	Daily dose	Duration			
1	10 cc.	2 days	Recovered	24 hrs. to recover	
2	10 cc.	2 days	Recovered	Dysentery suppressed after 48 hrs.	
3	10 c.c.	2 days	Recovered	24 hrs. to recover	
4	10 c.c.	2 days	Recovered	"	
5	10 c.c.	2 days	Recovered	"	
6	10 c.c.	3 days	Recovered	48 hrs. to recover	
7	10 c.c.	3 days	Recovered	"	
8	10 c.c.	3 days	Recovered	"	
9	10 c.c.	2 days	Recovered	24 hrs. to recover	
10	10 c.c.	4 days	Recovered	72 hrs. to recover	
11	10 c.c.	4 days	Recovered	"	
12	10 c.c.	3 days	Recovered	"	

It can be seen that all pigs recovered within 72 hours. Five of the animals recovered in 24 hours, four in 48 hours, and the remaining three animals in 72 hours. No secondary effects were detectable during this treatment.

### EXAMPLE III POLYARTHRITIS IN CALVES

It is well known that calves, when not duly cared for after birth, for instance by not taking all the hygienic measures which are recommended, generally suffer from an infection of the navel, which is called onphalophlebitis.

In view of the pain caused by this type of ailment, the animal prefers to lay down and stops eating, whereby its weight decreases very quickly and the animal gets weaker, to the extent of easily getting any other sickness.

This ailment is caused by pyogenic species of the genera Streptococcus, Staphylococcus and Escherichia Coli.

In order to carry out this experiment, two animals from the City of Naucalpan, State of Mexico, Mexico, were selected and treated with a 0.1% by weight solution of 1-bromo-3-chloro-5,5-dimethyl-hydantoin in water, by applying doses of 30 cc. through the intro-articular route in the form of a wash.

One of the calves which was badly affected by the ailment was cured after the first treat-

ment, while the other one was cured after the second treatment.

No side reaction was noticed in the above described treatments.

No more cases were reported in view of the fact that when disinfection of the cages where the remaining animals were placed, and the navels thereof, was effected, no other case of the above mentioned ailment occurred.

### EXAMPLE IV ESCHERICHIA COLI DIARRHEAS IN FATTENING CALVES

The effectiveness of the compositions in accordance with the present invention in combating diarrheas produced by different types of Escherichia Coli was tested. For this purpose 19 sick calves having an average weight of 60 kg. were selected (Naucalpan, State of Mexico, Mexico) and three daily doses of 50 c.c. each of an aqueous 0.033% 1-bromo-3-chloro-5,5-dimethyl-hydantoin solution were administered.

Most of the calves presented signs of cure on the second day of treatment, and the experiment was continued for 5 days at the above mentioned doses, with the result that out of the 19 calves treated, 18 responded to the treatment (95%) of which 16 were definitely cured after 5 days (84%) and 2 had

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responded to some extent to the treatment (11%), while only one of the calves did not respond to the above mentioned treatment, (5%).

- 5 After 9 days treatment, all the treated calves were cured and, even when relapses were found to have occurred, it was shown that these relapses were due to a source of reinfection, from extant bacteria in the water mixed 10 with the powdered milk which was fed to the calves.

In the above experiment it was shown that the 1-bromo-3-chloro-5,5-dimethyl-hydantoin administered at the foregoing doses, was highly effective for the treatment of *Escherichia Coli* diarrheas, and did not cause any side or secondary reaction.

Some of the calves of this Example had been previously treated with several wide spectrum antibiotics, without obtaining any satisfactory result.

#### EXAMPLE V AMOEBIASIS IN RATS

The present Example is given as an illustration of the usefulness of 1-bromo-3-chloro-5,5-dimethyl-hydantoin as an amoebicide.

For the present test three white rats weighing from 150 to 200 grams and a control rat weighing 156 grams were used.

30 The rats were inoculated with 50,000 trophozoites of *Endamoeba histolytica*, strain HSS, caecum. To do this the rats were anesthetized with ether, the skin of the ventral region was sterilized and depilated, and a surgical knife cut was effected in the medium line in order to uncover the caecum, within which the amoebae were introduced by means of a suitable syringe.

35 The wound was surgically closed and sterilized in order to avoid bacterial contamination.

The rats were placed in individual cages and after 5 days from inoculation, three of them received a dose of 30 mg/kg. by weight 45 of the animal of 1-bromo-3-chloro-5,5-dimethyl-hydantoin administered parenterally by means of a syringe.

After 7 days the rats were sacrificed and the 50 caecum region was observed, with the following results:

The control rat showed an ulcer in the

medium portion of this organ, covered with mucus which, upon examination under the microscope, presented abundant trophozoites of *Endamoeba histolytica*.

Two of the rats treated did not show any apparent injury and one of them showed an ulcerous injury located in the proximal region, but no amoeba could be found under the microscope. No amoebae were found in cuts examined under the microscope after dessicating the test specimen, fixing in Bouin liquid, and dyeing with hematoxylin-eosin. The injury gave the impression of an initial amoebic affection, which did not progress because the amoebae were exterminated by the 1-bromo-3-chloro-5,5-dimethyl-hydantoin used.

#### EXAMPLE VI TREATMENT OF INFECTIOUS DISEASES IN HUMANS

The present Example is intended to illustrate the great efficiency of 1-bromo-3-chloro-5,5-dimethyl-hydantoin when administered to human beings to combat several types of germs, particularly of the genera *Staphylococcus*, *streptococcus*, *Pneumococcus*, *Treponema*, *Trichomonas*, *Monilia* and *Shigella*.

In order to prove the foregoing, a series of experiments were effected using human beings of different ages, and administering any one of the three following formulations containing 1-bromo-3-chloro-5,5-dimethyl-hydantoin in the specified proportions: 0.1% by weight aqueous solution (GA); 0.01% by weight polyethylene glycol dispersion (GV); and 0.01% by weight polyethylene glycol dispersion containing 50,000 international units each of vitamins A and D (GVC).

In the following Table the above mentioned codes were used to represent the types of compositions administered in the treatment of each patient, and the results appear in a column, with "excellent" representing 100% cure; "good" 80%; "favorable" 60%; "poor" 40% or less; and "none" 0%.

It is to be noted that 1-bromo-3-chloro-5,5-dimethyl-hydantoin in any of the pharmaceutical forms used in these experiments, does not act through the skin, so that the abscesses were opened and the gums stripped before the compositions were applied.

TABLE III

Patient	Age and sex (Years)	Symptoms	Duration of the ailment	Therapy Daily Dosage and Duration	Results	Remarks
1	52—F	Purulent nasal flow, pain in the maxilar and frontal sinuses. Yellowish thick secretion in low amounts	3 months (sinusitis)	GA .. 3 drops in each nostril.	Excellent	Upon application, burning sensation of different intensity. After the first applica- tion the pain and congestion dis- appeared.
				GV .. 2 drops in each nostril.		
				2 times per day during 3 days		
				Dry sensation.		
				At the onset secretion increased.		
2	27—M	Constant pain which becomes acute period- ically in the frontal and maxilar sinuses, diffi- culty in breathing through the nose	12 years (sinusitis)	GA .. Spray and inspire 1 application	Excellent	Very intense burning sensation which dis- appeared after a few minutes
3	16—F	Pain in the maxilar sinuses, yellowish green scarce nasal flow. Impossibility in breath- ing through the nose.	10 days (sinusitis)	GA .. 2 drops in each nostril.	Good	The pain and the flow disappeared. The congestion only dis- appeared momentarily. Relief after 24 hrs.
				GV .. 2 drops in each nostril.		
				Every 5 hrs. for 1 day.		
4	38—M	Boils (Dermatitis)	4 days	GA .. Cleaning and external applica- tion for re- moving the false scar 24 hrs.	Excellent	The intradermic injuries were numerous, however, no pain noticeable upon application.

TABLE III (Continuation)

Patient	Age and sex (Years)	Symptoms	Duration of the ailment	Therapy Daily Dosage and Duration	Results	Remarks
5	48—F	Acute pain in a molar tooth with caries	(4th degree caries) 2 days	GV ..	External medicinal application in the caries. Reposition after 10 hrs. 1 day	Excellent
6	68—M	Intense and constant pain in the throat. Difficulty in swallowing. The patient has suffered from the above for several years and this ailment became acute recently. Dark red mucus with coagulations resembling small abscesses.	Pharyngitis 5 days	GA ..	Throat wash every 5 hrs. (4 times per day during 2 days)	Excellent The pain ceased after 10 minutes and the inflammation also ceased. Extraction of the tooth.
7	94—F	Pain in the throat very reddened and ulcerated mucosa. Aphonia. (Chronic ailment in the acute face).	Ulcerous laryngitis and pharyngitis 2 years	GA .. GVC..	Throat wash External application. 3 times per day during 2 days	Good After one month the ulceration was again present (old age).
8	12—M	(Deaf and dumb) Pain and suppuration from an ear. Chronic ailment. (Fecidity)	Suppurated otitis. 4 years	GA .. GV ..	Washing, 2 times a day 2 drops, 3 times a day during 6 days.	The pain disappeared
9	44—M	Pain in the rear portion of the last molar; varicose vein, highly enlarged and painful periodically.	Varix 20 years	GVC ..	External application 2 times a day (1 day)	Excellent Resistant to treatment with iodine and astringent agents externally applied.

TABLE III (Continuation)

Patient	Age and sex (Years)	Symptoms	Duration of the ailment	Therapy Daily Dosage and Duration	Results	Remarks
10	34—F	Vaginal flow, brown color, burning sensation and pain. (Trichomoniasis, accompanied with monilia and staphylococcus).	2 years	GA .. Wash with a tablet of 500 mg. of vitamin C. (vaginal shower of 250 ml.) 1 day.	Excellent	Slight burning sensation which disappeared after a few minutes.
11	5—F	Frequent evacuation with blood. (Bagerness and tenesmus) resistant to chloromyacin previously prescribed.	8 days	GA .. Diluted to one third. One spoonful after each meal. (3 times per day). 3 days.	Excellent	The intestinal flora was reinstated with yeast Z—37. One ampule daily.
12	5—F	Fetid diarrhea, tenesmus and eagerness	Colitis 3 days	GA .. 1 spoonful 3 times a day (after each meal) (Dilution to one third). 24 hrs.	Excellent	Reposition of the intestinal flora with yeast Z—37. One ampule daily (2).
13	10—M	Fetid evacuation, rattling noise pyrexia 39°C. Intestinal pain.	Salmonellosis 6 days (No laboratory examinations were effected)	GA .. Diluted to one third, 1 spoonful each 4 hrs. (Meals: juices, gelatines) 5 days,	Excellent	After the third day pyrexia disappeared and evacuations were modified. The intestinal flora was reinstated with yeast Z—37. 1 ampule daily (5).

TABLE III (Continuation)

Patient	Age and sex (Years)	Symptoms	Duration of the ailment	Therapy Daily Dosage and Duration	Results	Remarks
14	58—M	Surgical wound (skin and subcutaneous cellular tissue injured)	Wound 1 day	GV .. Drops in the wound before saturation. 1 time.	Excellent	No pain, slight burning sensation which disappeared within the same day.
15	44—M	Burning sensation, irritation in the eyelids with purulent closed and open abscesses. Itching and pain.	Blepharitis 19 years Neisseria C.	GA .. Diluted 1/2, 3 times a day. Wash 2 days.	Good	The symptoms and open abscesses dis- appeared and only the closed abscesses remained.
16	63—M	Burning sensation and conjunctive irritation, purulent secretion	Conjunctivitis 2 days	GA .. Diluted 1/2. Wash 3 times per day. 1 day	Excellent	Slight burning sen- sation with the washings which dis- appeared after a few minutes.
17	17—F	Numerous cutaneous abscesses	Facial Pimples 15 days	GA .. Diluted 1/2 Drops and washings 2 times times a day	Favorable	The open abscesses disappeared and only those which could not be pressed re- mained.

5 The following Examples illustrate some tests effected *in vitro* to show the action of chloro-bromodimethyl-hydantoin against different pathogenic microorganisms extensively attacking men and animals.

**EXAMPLE VII  
ESHERICHIA COLI**

A.— An aqueous 1.05% by weight solution of 1-bromo-3-chloro-5,5-dimethyl hyd-

toin was prepared, and dilutions were effected 10 from this mother solution, and placed in amounts of 1 ml. together with 1 ml. of a suspension of Esch. Coli (131,000,000/ml.) (after 19 hours of incubation). Suitable amounts of nutrient broth were added in order to bring 15 the volume to 10 ml. The final concentration of 1-bromo-3-chloro-5,5-dimethyl-hydantoin in each of the tubes is as follows:

Eschericia Coli	Results	
	Incubation 48 hours	
131,000,000	Tube No. 1 .000105 g./ml.	Growth
	Tube No. 2 .000210 „	No growth
	Tube No. 3 .000315 „	No growth
	Tube No. 4 .000420 „	No growth
	Tube No. 5 .000525 „	No growth

20 B.— A set of control tubes was prepared, into which 8 ml. of nutrient broth, 1 ml. of the suspension of E. Coli and 1 ml. of isotonic serum were introduced. The tubes were incubated for 48 hours, at the end of which period 25 growth was found only in tube No. 1 while no growth could be found in all of the remaining control tubes. In order to check the results, a reseeding was made from the tube treated to new culture medium, and incubation was carried out for 48 hours more, where-

after growth was found only in the first tube again.

**EXAMPLE VIII  
STAPHYLOCOCCUS AUREUS**

A strain, seeded in nutrient agar, was incubated for 24 hours to give a concentration of 355 millions per ml.

1 ml. of the above mentioned strain was placed in 1 ml. of a dilute solution of 1-bromo-3-chloro-5,5-dimethyl-hydantoin in nutrient 40 broth medium.

**Concentrations of the Dilutions of 1-Bromo-3-Chloro-5,5-Dimethyl-Hydantoin**

Tube No. 1	0.000210 g. per ml.
Tube No. 2	0.000315 g. per ml.
Tube No. 3	0.000420 g. per ml.
Tube No. 4	0.000525 g. per ml.
Tube No. 5	0.000630 g. per ml.

45 The tubes were incubated at 37°C. for 60 hours. After this period of time no growth could be detected in Tube No. 2, that is, for a strain of 355 millions per ml. a total inhibition is caused by a concentration of 315 micrograms of 1-bromo-3-chloro-5,5-dimethyl-hydantoin.

50 **EXAMPLE IX  
BRUCELLA ABORTUS**

TEST NO. 1  
A saturated solution of 1-bromo-3-chloro-

5,5-dimethyl-hydantoin in distilled water was prepared, and from this mother solution the following dilutions were effected and placed in a suspension of Brucella abortus having 357,000,000,000 microorganisms (culture after 24 hours incubation). The microorganisms were seeded in a 1% peptone medium and incubated for 48 hours, to thereby obtain the following results:

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Tube No. 1	Growth	0.000000000105 g/ml.
Tube No. 2	"	0.000000000105 g/ml.
Tube No. 3	"	0.000000000105 g/ml.
Tube No. 4	"	0.000000000105 g/ml.
Tube No. 5	"	0.000000000105 g/ml.
Tube No. 6	"	0.000000000105 g/ml.
Tube No. 7	"	0.000000000105 g/ml.
Tube No. 8	"	0.000000000105 g/ml.
Tube No. 9	"	0.000000000105 g/ml.
Tube No. 10	No growth	0.0105 g/ml.

From the above it can be concluded that dilutions with a concentration lower than 0.00105 g/ml. do not act on Brucella abortus, but that a concentration of 0.0105 g/ml. completely inhibits a culture of B. abortus having 357,000,000,000 microorganisms.

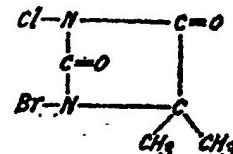
directly studied. No 1-bromo-3-chloro-5,5-dimethyl-hydantoin was found in any of the organs in the form of a therapeutically active composition.

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#### WHAT I CLAIM IS:—

1. A wide spectrum germicidal therapeutic composition for use in combating infectious diseases in warm-blooded animals, including humans, comprising a germicidally active proportion of 1-bromo-3-chloro-5,5-dimethyl-hydantoin of the formula:—

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and a pharmacologically acceptable carrier therefor, but excluding solutions of the hydantoin in water or an organic solvent.

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2. A germicidal composition according to claim 1 in which the carrier is a polyalkylene glycol.

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3. A germicidal composition according to claim 2 in which the polyalkylene glycol is polyethylene glycol.

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4. A germicidal composition according to claim 2 in which the polyalkylene glycol is polypropylene glycol.

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5. A germicidal composition according to claim 2 in which the polyalkylene glycol is a polybutylene glycol.

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6. A germicidal composition according to claim 1 in which the carrier is an aqueous medium comprising water and vitamins A and D.

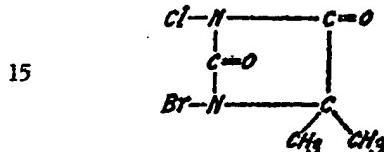
7. A germicidal composition according to any one of claims 1 to 6 in which the proportion of 1-bromo-3-chloro-5,5-dimethyl-hydan-

- EXAMPLE X  
SALMONELLA AND SHIGELLA
- 10 By seeding 1 ml. of suspension of germs at the concentrations hereunder listed, together with 1 ml. of 1-bromo-3-chloro-5,5-dimethyl-hydantoin solution at a concentration of 0.0001 g/ml. in nutrient agar and incubating at 37°C. for 48 hours, a total inhibition was found to occur on:
- 15 200 000 colonies/ml. of Salmonella paratyphi A
- 20 100 000 colonies/ml. of Salmonella paratyphi B
- 200 000 colonies/ml. of Salmonella typhi
- 200 000 colonies/ml. of Shigella Sonne
- All the above Examples show that 1-bromo-25 3-chloro-5,5-dimethyl-hydantoin, in the form of therapeutic compositions of matter, was highly effective in combating numerous veterinary and human ailments.
- The amount of 1-bromo-3-chloro-5,5-di-30 methyl hydantoin retained by the body is negligible, which constitutes another remarkable advantage in relation to prior art medications used for curing infectious ailments.
- The fact that the 1-bromo-3-chloro-5,5-di-35 methyl hydantoin is not retained by the body after it has been applied to organs can be proved by carrying out numerous experiments in rats using stomach probes for prolonged periods of time. After the 1-bromo-3-chloro-5,5-dimethyl-hydantoin had been applied, different functional tests were made on the rats and the rats were then killed and their organs

toin is from 0.005 to 1.0% by weight with respect to the total weight of the composition.

8. A composition as claimed in claim 7, in which the proportion of 1-bromo-3-chloro-5,5-dimethyl-hydantoin is 0.01% by weight with respect to the total weight of the hydantoin and carrier and the carrier is an oily vehicle.

9. A method for treating germ-caused ailments in non-human warm-blooded animals, which comprises administering parenterally, topically or orally to the animal a germicidal amount of 1-bromo-3-chloro-5,5-dimethylhydantoin of the formula:



in a pharmacologically acceptable carrier.

10. A method according to claim 9 in which the proportion of 1-bromo-3-chloro-5,5-

dimethyl-hydantoin is from 0.005% to 1.0% by weight with respect to the total weight of 20 the hydantoin and carrier.

11. A method according to claim 9 or 10 in which the carrier is a polyalkylene glycol.

12. A method according to claim 9 or 10 in which the carrier is an aqueous medium.

13. A method according to any one of claims 9 to 12 in which the 1-bromo-3-chloro-5,5-dimethyl-hydantoin is administered topically together with vitamins A and D.

14. A method for curing mastitis in non-human animals which comprises administering to the sick animals, through the intra-mammary route, 0.01% by weight of 1-bromo-3-chloro-5,5-dimethyl-hydantoin dispersed in polyethylene glycol.

15. Germicidal compositions according to claim 1 substantially as hereinbefore described in the Examples.

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